

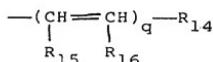
species. In the Office Action of February 26, 1986, election of a single disclosed species was required. The election was made in compliance with 37 CFR 1.146 and action in accordance with MPEP 809.02(c) is believed to be appropriate with respect to Claims 9 and 19-22.

Claims 1, 3-5, 10-13 and 15-18 are rejected under 35 USC 103 over Hamberger et al. (of record). The Examiner indicates that the Hamberger reference discloses compounds in which the various "R" groups can be the same as those set out in the instant claims. The Examiner notes, for example, that R₁ can be naphthyl and R₆ can be alkenyl or alkynyl. The Examiner indicates, in addition, that the prior art compounds have the same activities as Applicant's compounds. The Examiner concludes that no invention is apparent in the presently claimed compounds, compositions and the method of use in the absence of unexpected properties. Applicant respectfully disagrees and traverses the objection.

As noted by the Examiner, certain subject matter now claimed, in which substituent R₁ is naphthyl (group IIa) or groups IIb, IID or IIh and substituent R₆ is a group of the formula IIIa

$$(-C\equiv C-R_{11}) ,$$

can be constructed from the broad generic language of the Hamberger reference. Hamberger, however, does not disclose any compounds which contain the IIIa group. The pertinent section of the Hamberger reference is definition (v) for substituent R₆ on Page 4 and in Claim 1. The substituent is defined there as a radical of the formula IIIf:



wherein R_{14} is lower alkyl, alkoxy (C_{1-12})carbonyl, alkenyl (C_{3-12}), alkynyl (C_{3-12}), phenylalkyl (C_{7-12}) or phenyl,

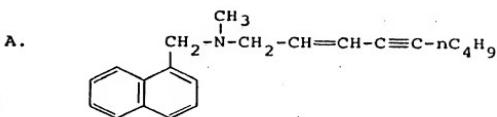
R_{15} and R_{16} , independently, are hydrogen or lower alkyl,

and q is a whole number from 0 to 5.

Applicant's closest IIIa compounds, the compounds in which R_{11} is alkyl, can be obtained from the definition of the Hamberger R_6 substituent by selecting as R_6 a radical of formula IIIf in which q is 0 and R_{14} is (C_{3-12})alkynyl. It is clear from the breadth of the reference, however, that this selection could only be made with direction from the instant application. The Hamberger reference itself does not suggest any compounds which are even remotely related to the presently claimed alkynyl compounds. The only comment concerning the R_{14} substituent in Hamberger is on Page 7, lines 1 to 3, where the reference indicates that " R_{14} is conveniently alkoxy(C_{1-8})carbonyl, phenyl or alkyl or phenalkyl." The reference further indicates on Page 5, lines 21-23, that any multiple bond is preferably not in the α -or β -position but is at the remote terminal position of substituent R_6 . In the present compounds, the alkynyl bond is in the α -position of R_6 , that is, in the position nearest the point of substitution. The teachings of Hamberger, therefore, not only do not suggest Applicant's compounds, they, in fact, lead away from them. It is only by picking and choosing from the broad language of the reference, guided by the teachings of the instant application, that one is able to construct the presently claimed compounds. There is no way that one skilled in the

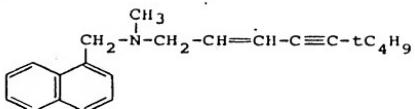
art using the Hamberger preferences and examples would be logically led to Applicant's compounds. The Court of Customs and Patent Appeals indicated In re Taborsky (183 USPQ 50), that for obviousness, the prior art must provide one with motivation to make the molecular modifications needed to arrive at the claimed compounds. In the present case, there is nothing in Hamberger which would motivate one to make the selections required to obtain the instant compounds.

In support of the patentability of the alkynyl compounds now claimed, Applicant is enclosing a Declaration under Rule 132 (37 CFR 1.132), which compares the activity of Applicant's alkynyl derivatives with the closest compounds disclosed in the Hamberger reference, namely, the corresponding alkenyl derivatives. These alkenyls are the next adjacent unsaturated derivatives to Applicant's compounds and have the $\alpha=1$ and $R_{14}=\text{alkyl}$ (*n*-butyl) or phenyl preferences set out at the bottom of Page 6 and top of Page 7 of the Hamberger application. There are no closer compounds disclosed in the reference. The United States patent application corresponding to the Hamberger application, Serial No. 934,772, filed August 18, 1978, contains further exemplification; but the additional compounds are even more remote than the alkenyls of the Declaration. The compounds compared are the Example 3, (Claim 9), 16 (Claim 10) and 18 (Claim 19a) compounds from the present application and the Examples 16 and 17 compounds from the Hamberger et al. European Application. These compounds have the following structures:



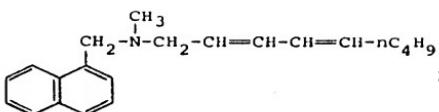
US Ser.No. 233,559
Example 3
Claim 9

B.



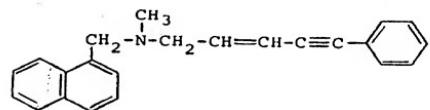
US Ser. No. 233,559
Example 16
Claim 10

(i)



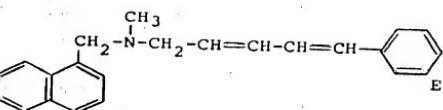
EP Appln. No. 896
Example 17

C.



US Ser. No. 233,559
Example 18
Claim 19a

(ii)



EP Appln. No. 896
Example 16

The results in the Declaration show that Applicant's Claim 9 compound A is approximately 2 to 8 times more active than reference compound (i) against the strains numbered 158, 150, 167, 177 and 39; and that the elected compound B is approximately 4 to 60 times more active than (i) against all strains tested except Candida albicans 124. Applicant's Claim 19a compound C is approximately 4 to 16 times more active than the closest Hamberger compound (ii) against strains 158, 150, and 167. These increases in activity are clearly completely unexpected, as indicated by the Declarant, especially in light of the preferences in the Hamberger reference. Applicant submits that the Declaration clearly rebuts any presumption of obviousness for the compounds of present Claim 9, 10, and 19a and that these compounds are certainly patentable.

over the Hamberger et al. reference.

With respect to remaining compounds in which R₆ is the alkynyl group, IIIa or the cycloalkylidinyl group IIIC, there is nothing in Hamberger which would suggest or lead one skilled in the art to these more remote compounds. Hamberger discloses only compounds in which R₁₄ is alkyl or phenyl; and, therefore, the alkyl and phenyl compounds of the showing are commensurate with the scope of the prior art. The Declaration shows that it is the specific alignment of the alkynyl and alkenyl moieties in the IIIa compound that confers unexpected superiority over the closest compounds of the art. Accordingly, all of the presently claimed compounds are patentable over the Hamberger European Application; and, therefore, it is respectfully requested that the Examiner reconsider the instant rejection under 35 USC 103 and withdraw it.

Applicant notes that the Examiner has not acknowledged the Claim of Priority under 35 USC 119 submitted with the communication of March 24, 1986. It is assumed that this was overlooked by the Examiner and that the acknowledgment will be made in the next Office Action.

In view of the above amendments and comments, it is believed that the instant application is now in condition for allowance, and accordingly, it is respectfully requested that the Examiner withdraw the rejection of the application and pass the application to issue.

Respectfully submitted,

ANTON STUETZ

Thomas O'Malley
Thomas O. McGovern
Agent for Applicant
Reg. No. 25,741
(201) 386-8580

SANDOZ CORP.
59 Route 10
E. Hanover, NJ 07936

TON/vls
September 24, 1986

Encl.: Declaration Under Rule 132
Postcard